

Naval Medical Center Portsmouth (NMCP) COVID-19 Literature Report

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, special reports, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Due to the rapid evolution of the literature, I will not update past reports when new information arises; for retracted papers specific to COVID-19, see the [list of retracted papers from Retraction Watch](#).

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A Brief Note and Request

The NMCP COVID-19 Literature Report has been produced for over 2 years. These reports take significant time and effort to produce. As the 100th issue approaches, I want to touch base with the people who read the reports and ask:

- What value do these reports have to you? Have they made a difference in decision making or impacted patient care?
- Should these reports continue? If they do, how can they best support what you need?

I welcome your opinions, suggestions, or any other constructive feedback regarding these reports (email usn.hampton-roads.navhosp@va.gov). Thank you!

The Big Picture

News in Brief

"COVID death tolls: scientists acknowledge errors in WHO estimates" ([Nature](#)).

"Going viral? Implications of COVID-19 for bioterrorism" ([CTC Sentinel \[pdf\]](#)).

Misinformation

"Journal runs editorial fraught with COVID misinformation — Epidemiologist calls its conjecture 'bizarre' and 'astonishingly unscientific'" ([Medpage](#)).

Long Reads

"Hard hit by COVID-19, Black Americans are recovering slowly — Experts say it will take longer for Black communities to recover from the pandemic's public health and economic impact" ([NatGeo](#)).

Webinars and Other Events

WHAT: Medical, Biomedical & Biodefense: Support to the Warfighter Symposium (hosted by Offices of Senator Richard Burr, Senator Thom Tillis, the North Carolina Military Business Center, and the North Carolina Biotechnology Center)

WHEN: 08-09 June 2022

WHERE: In person at University of North Carolina, The Friday Center, Chapel Hill, NC

MORE INFO: <https://mbb.ncmbc.us/event-info/>

Special Reports and Other Resources

ARMI: [Essential Medicines Supply Chain and Manufacturing Resilience Assessment \[pdf\]](#) (May 2022)

"Led by the U.S. Department of Health and Human Services (HHS) Office of the Assistant Secretary for Preparedness and Response and ARMI's Next Foundry for American Biotechnology (NextFAB), the Essential Medicines Supply Chain and Manufacturing Resilience Assessment report outlines the supply chain vulnerabilities – specifically those affecting critical medicines on the FDA's Essential Medicines List."

Journal Articles

JAMA Netw Open: [Changes in Cancer Screening in the US During the COVID-19 Pandemic](#) (03 June 2022)

"Question: Did the national prevalence of breast, cervical, and colorectal cancer screening change during the COVID-19 pandemic?

Findings: In this national survey study, between 2018 and 2020, past-year breast and cervical cancer screening prevalence declined by 6% and 11%, respectively. There was no change in past-year colorectal cancer screening prevalence, with a 7% increase in stool testing and a 16% decrease in colonoscopy.

Meaning: These findings suggest that stool testing counterbalanced decreases in colonoscopy during 2020, whereas breast and cervical cancer screening decreased modestly."

Eur Heart J: [The collateral damage of COVID-19 to cardiovascular services: a meta-analysis](#) (30 May 2022)

"Aims: The effect of the COVID-19 pandemic on care and outcomes across non-COVID-19 cardiovascular (CV) diseases is unknown. A systematic review and meta-analysis was performed to quantify the effect and investigate for variation by CV disease, geographic region, country income classification and the time course of the pandemic.

Methods and results: From January 2019 to December 2021, Medline and Embase databases were searched for observational studies comparing a pandemic and pre-pandemic period with relation to CV disease hospitalisations, diagnostic and interventional procedures, outpatient consultations, and mortality. Observational data were synthesised by incidence rate ratios (IRR) and risk ratios (RR) for binary outcomes and weighted mean differences for continuous outcomes with 95% confidence intervals. The study was registered with PROSPERO (CRD42021265930). A total of 158 studies, covering 49 countries

and 6 continents, were used for quantitative synthesis. Most studies (80%) reported information for high-income countries (HICs). Across all CV disease and geographies there were fewer hospitalisations, diagnostic and interventional procedures, and outpatient consultations during the pandemic. By meta-regression, in low-middle income countries (LMICs) compared to HICs the decline in ST-segment elevation myocardial infarction (STEMI) hospitalisations (RR 0.79, 95% confidence interval [CI] 0.66–0.94) and revascularisation (RR 0.73, 95% CI 0.62–0.87) was more severe. In LMICs, but not HICs, in-hospital mortality increased for STEMI (RR 1.22, 95% CI 1.10–1.37) and heart failure (RR 1.08, 95% CI 1.04–1.12). The magnitude of decline in hospitalisations for CV diseases did not differ between the first and second wave.

Conclusions: There was substantial global collateral CV damage during the COVID-19 pandemic with disparity in severity by country income classification."

JAMA Netw Open: [Association of Zip Code Vaccination Rate With COVID-19 Mortality in Chicago, Illinois](#) (27 May 2022)

"Question: What was the association of vaccination coverage inequity with COVID-19 mortality in Chicago, Illinois?

Findings: In this cohort study of 2 686 355 Chicago residents, higher zip code vaccination coverage was associated with lower relative risks of death during the Alpha and Delta waves of the COVID-19 pandemic. Approximately 75% of deaths in the least vaccinated zip codes may have been prevented if mortality trends had remained parallel with the most vaccinated zip codes.

Meaning: These findings suggest that low zip code–level vaccination rates in Chicago were associated with more deaths in the Alpha and Delta waves, exacerbating racial and ethnic disparities in COVID-19 mortality."

COVID-19 Vaccines

News in Brief

"Moderna seeking FDA authorization of omicron-specific booster shot" ([WP](#)).

"Moderna says its new vaccine booster shows 'superior' response to omicron" ([NPR](#)).

"A more traditional coronavirus shot on the way for some unable to wait" ([WP](#)).

Journal Articles

MMWR: [COVID-19 Vaccination Coverage, by Race and Ethnicity — National Immunization Survey Adult COVID Module, United States, December 2020–November 2021](#) (10 June 2022)

"What is already known about this topic? Racial and ethnic minority groups have been disproportionately affected by the COVID-19 pandemic. Vaccination is effective in preventing COVID-19 infection and severe illness, and equitable vaccine administration can reduce COVID-19–related disparities.

What is added by this report? Asian and non-Hispanic White adults had the highest COVID-19 vaccination coverage by the end of April 2021. By the end of November 2021, disparities in vaccination coverage for some racial and ethnic groups narrowed, and coverage was similar for non-Hispanic Black (78.2%), Hispanic (81.3%), Native Hawaiian and other Pacific Islander (75.7%), and non-Hispanic White (78.7%) adults.

What are the implications for public health practice? Equitable access to and receipt of COVID-19 vaccination, including booster doses, is critical to reducing racial and ethnic disparities in vaccination."

Clin Infect Dis: [Immunogenicity of a third dose of BNT162b2 to ancestral SARS-CoV-2 & Omicron variant in adults who received two doses of inactivated vaccine](#) (08 June 2022)

"Background: Limited data exist on antibody responses to mixed vaccination strategies involving inactivated COVID-19 vaccines, particularly in the context of emerging variants.

Methods: We conducted an open label trial of a third vaccine dose of an mRNA vaccine (BNT162b2, Fosun Pharma/BioNTech) in adults aged ≥ 30 years who had previously received two doses of inactivated COVID-19 vaccine. We collected blood samples before administering the third dose and 28 days later, and tested for antibodies to the ancestral virus using a binding assay (ELISA), a surrogate virus neutralization test (sVNT) and a live virus plaque reduction neutralization test (PRNT). We also tested for antibodies against the Omicron variant using live-virus PRNT.

Results: In 315 participants, a third dose of BNT162b2 substantially increased antibody titers on each assay. Mean ELISA levels increased from an optical density (OD) of 0.3 to 2.2 ($p < 0.001$), and mean sVNT levels increased from an inhibition of 17% to 96% ($p < 0.001$). In a random subset of 20 participants, the geometric mean PRNT50 titers rose very substantially by 45 fold from Day 0 to Day 28 against the ancestral virus ($p < 0.001$) and rose by 11 fold against the Omicron variant ($p < 0.001$). In daily monitoring, post-vaccination reactions subsided within 7 days for over 99% of participants.

Conclusions: A third dose of COVID-19 vaccination with an mRNA vaccine substantially improved antibody levels against the ancestral virus and the Omicron variant with well-

tolerated safety profile, in adults who had received two doses of inactivated vaccine 6 months earlier."

Clin Infect Dis: [Durability of SARS-CoV-2 mRNA Booster Vaccine Protection Against Omicron Among Health Care Workers with a Vaccine Mandate](#) (06 June 2022)

"Background: The SARS-CoV-2 Omicron Variant has spread rapidly throughout the world since being identified in South Africa in November 2021. Few studies have assessed primary series and booster vaccine effectiveness against Omicron among US health care workers.

Methods: We conducted a test-negative case-control design to estimate BNT162b2 and mRNA1273 primary vaccination and booster effectiveness against SARS-CoV-2 infection and symptomatic Covid-19 during an Omicron surge among employees of the University of Pennsylvania Health System. The study period was between 7/1/21-4/5/22. We defined the Delta period as 7/1/21-12/12/21 and the Omicron period as beginning 12/20/21.

Results: Our sample included 14,520 tests (2,776 [19%] positive)-7,422 (506 [7%] positive) during Delta, and 7,098 (2270 [32%] positive) during Omicron. Benchmarked against Delta, vaccine effectiveness of two vaccine doses was lower during Omicron, with no significant protection against infection. Booster doses added significant protection, although they also showed reduced effectiveness during Omicron. Compared to employees who had received two vaccine doses, three BNT162b2 doses had a relative effectiveness of 50% (95% CI 42-56%) during Omicron, relative to 78% (95% CI 63-87%) during Delta; three mRNA1273 doses had a relative effectiveness of 56% (95% CI 45-65%) during Omicron, relative to 96% (95% CI 82-99%) during Delta. Restricting the sample to symptomatic tests yielded similar results to our primary analysis. After initial waning in BNT162b2 booster protection against infection, it remained largely stable for at least 16 weeks after vaccination.

Discussion: Our findings provide a strong rationale for boosters among healthcare workers in the Omicron era."

NEJM: [Efficacy and Safety of a Recombinant Plant-Based Adjuvanted Covid-19 Vaccine](#) (02 June 2022)

"Background: Coronavirus-like particles (CoVLP) that are produced in plants and display the prefusion spike glycoprotein of the original strain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are combined with an adjuvant (Adjuvant System 03 [AS03]) to form the candidate vaccine.

Methods: In this phase 3, multinational, randomized, placebo-controlled trial conducted at 85 centers, we assigned adults (≥ 18 years of age) in a 1:1 ratio to receive two intramuscular injections of the CoVLP+AS03 vaccine or placebo 21 days apart. The primary objective of the trial was to determine the efficacy of the CoVLP+AS03 vaccine in preventing symptomatic

coronavirus disease 2019 (Covid-19) beginning at least 7 days after the second injection, with the analysis performed after the detection of at least 160 cases.

Results: A total of 24,141 volunteers participated in the trial; the median age of the participants was 29 years. Covid-19 was confirmed by polymerase-chain-reaction assay in 165 participants in the intention-to-treat population; all viral samples that could be sequenced contained variants of the original strain. Vaccine efficacy was 69.5% (95% confidence interval [CI], 56.7 to 78.8) against any symptomatic Covid-19 caused by five variants that were identified by sequencing. In a post hoc analysis, vaccine efficacy was 78.8% (95% CI, 55.8 to 90.8) against moderate-to-severe disease and 74.0% (95% CI, 62.1 to 82.5) among the participants who were seronegative at baseline. No severe cases of Covid-19 occurred in the vaccine group, in which the median viral load for breakthrough cases was lower than that in the placebo group by a factor of more than 100. Solicited adverse events were mostly mild or moderate and transient and were more frequent in the vaccine group than in the placebo group; local adverse events occurred in 92.3% and 45.5% of participants, respectively, and systemic adverse events in 87.3% and 65.0%. The incidence of unsolicited adverse events was similar in the two groups up to 21 days after each dose (22.7% and 20.4%) and from day 43 through day 201 (4.2% and 4.0%).

Conclusions: The CoVLP+AS03 vaccine was effective in preventing Covid-19 caused by a spectrum of variants, with efficacy ranging from 69.5% against symptomatic infection to 78.8% against moderate-to-severe disease."

BMJ: [Effectiveness of heterologous and homologous covid-19 vaccine regimens: living systematic review with network meta-analysis](#) (31 May 2022)

"Objective: To evaluate the effectiveness of heterologous and homologous covid-19 vaccine regimens with and without boosting in preventing covid-19 related infection, hospital admission, and death.

Design: Living systematic review and network meta-analysis.

Data sources: World Health Organization covid-19 databases, including 38 sources of published studies and preprints.

Study selection: Randomised controlled trials, cohort studies, and case-control studies.

Methods: 38 WHO covid-19 databases were searched on a weekly basis from 8 March 2022. Studies that assessed the effectiveness of heterologous and homologous covid-19 vaccine regimens with or without a booster were identified. Studies were eligible when they reported the number of documented, symptomatic, severe covid-19 infections, covid-19 related hospital admissions, or covid-19 related deaths among populations that were vaccinated and unvaccinated. The primary measure was vaccine effectiveness calculated as 1-odds ratio. Secondary measures were surface under the cumulative ranking curve

(SUCRA) scores and the relative effects for pairwise comparisons. The risk of bias was evaluated by using the risk of bias in non-randomised studies of interventions (ROBINS-I) tool for all cohort and case-control studies. The Cochrane risk of bias tool (version 2; ROB-2) was used to assess randomised controlled trials.

Results: The first round of the analysis comprised 53 studies. 24 combinations of covid-19 vaccine regimens were identified, of which a three dose mRNA regimen was found to be the most effective against asymptomatic and symptomatic covid-19 infections (vaccine effectiveness 96%, 95% credible interval 72% to 99%). Heterologous boosting using two dose adenovirus vector vaccines with one mRNA vaccine has a satisfactory vaccine effectiveness of 88% (59% to 97%). A homologous two dose mRNA regimen has a vaccine effectiveness of 99% (79% to 100%) in the prevention of severe covid-19 infections. Three dose mRNA is the most effective in reducing covid-19 related hospital admission (95%, 90% to 97%). The vaccine effectiveness against death in people who received three doses of mRNA vaccine remains uncertain owing to confounders. In the subgroup analyses, a three dose regimen is similarly effective in all age groups, even in the older population (≥ 65 years). A three dose mRNA regimen works comparably well in patients who are immunocompromised and those who are non-immunocompromised. Homologous and heterologous three dose regimens are effective in preventing infection by covid-19 variants (alpha, delta, and omicron).

Conclusion: An mRNA booster is recommended to supplement any primary vaccine course. Heterologous and homologous three dose regimens work comparably well in preventing covid-19 infections, even against different variants. The effectiveness of three dose vaccine regimens against covid-19 related death remains uncertain."

Transmission, Exposure, and Surveillance

News in Brief

"This photo of a professor wearing a mask went viral. So did his response to critics" ([NPR](#)).

Variants

"Why call it BA.2.12.1? A guide to the tangled Omicron family" ([Nature](#)).

"Dominant coronavirus mutant contains ghost of pandemic past" ([AP](#)).

Long Reads

"Behind the high-tech COVID-19 tests you probably haven't heard about — OTC molecular tests combine PCR accuracy with the convenience of rapid antigen tests" ([Verge](#)).

"Tracking coronavirus in animals takes on new urgency — Inside the global hunt to identify mutations that might lead to more lethal variants" ([WP](#); includes audio option).

Journal Articles

Clin Infect Dis: [SARS-CoV-2 Outbreak at a College with High COVID-19 Vaccination Coverage-Connecticut, August-September 2021](#) (08 June 2022)

"Background: During August-September 2021, a Connecticut college experienced a large SARS-CoV-2 Delta outbreak despite high (99%) vaccination coverage, indoor masking policies, and twice weekly reverse transcription-polymerase chain reaction (RT-PCR) testing. The Connecticut Department of Public Health investigated characteristics associated with infection and phylogenetic relationships among cases.

Methods: A case was a SARS-CoV-2 infection diagnosed by RT-PCR or antigen test during August-September 2021 in a student. College staff provided enrollment data, case information, and class rosters. An anonymous online student survey collected demographics, SARS-CoV-2 case and vaccination history, and activities the weekend before the outbreak. Multivariate logistic regression identified characteristics associated with infection. Phylogenetic analyses compared 115 student viral genome sequences with contemporaneous community genomes.

Results: Overall, 199/1788 students (11%) had lab-confirmed SARS-CoV-2 infection; most were fully vaccinated (194/199, 97%). Attack rates were highest among sophomores (72/414, 17%) and unvaccinated students (5/18, 28%). Attending in-person classes with an infectious student was not associated with infection (adjusted odds ratio [aOR] 1.0; 95%CI 0.5-2.2). Compared with uninfected students, students reporting an infection were more likely sophomores (aOR 3.3; 95%CI 1.1-10.7), attended parties/gatherings before the outbreak (aOR 2.8; 95%CI 1.3-6.4), and completed a vaccine series ≥ 180 days prior (aOR 5.5; 95%CI 1.8-16.2). Phylogenetic analyses suggested most cases derived from a common viral source.

Conclusions: This college SARS-CoV-2 outbreak occurred in a highly vaccinated population with prevention strategies in place. Infection was associated with unmasked off-campus parties/gatherings, not in-person classes. Students should stay up-to-date on vaccination to reduce infection."

JAMA Netw Open: [Concordance of SARS-CoV-2 RNA in Aerosols From a Nurses Station and in Nurses and Patients During a Hospital Ward Outbreak](#) (08 June 2022)

"Question: Is SARS-CoV-2 RNA found in aerosols in hospital break rooms and nurses stations during a nosocomial outbreak?

Findings: In this cohort study, SARS-CoV-2 genome sequences in air samples collected at a nurses station were identified in all particle sizes and were identical to human samples from a nosocomial outbreak. Detection of aerosol-borne SARS-CoV-2 was statistically less frequent on units under surveillance (7 of 210 samples) than without surveillance (24 of 300 samples).

Meaning: These findings suggest that nosocomial infection may result from aerosol-borne SARS-CoV-2 introduced by employees and patients into common hospital areas; surveillance may help reduce the introduction of SARS-CoV-2 into aerosols."

PLoS One: [Diagnostic accuracy of non-invasive detection of SARS-CoV-2 infection by canine olfaction](#) (01 June 2022)

"Background: Throughout the COVID-19 pandemic, testing individuals remains a key action. One approach to rapid testing is to consider the olfactory capacities of trained detection dogs.

Methods: Prospective cohort study in two community COVID-19 screening centers. Two nasopharyngeal swabs (NPS), one saliva and one sweat samples were simultaneously collected. The dog handlers (and the dogs...) were blinded with regards to the Covid status. The diagnostic accuracy of non-invasive detection of SARS-CoV-2 infection by canine olfaction was assessed as compared to nasopharyngeal RT-PCR as the reference standard, saliva RT-PCR and nasopharyngeal antigen testing.

Results: 335 ambulatory adults (143 symptomatic and 192 asymptomatic) were included. Overall, 109/335 participants tested positive on nasopharyngeal RT-PCR either in symptomatic (78/143) or in asymptomatic participants (31/192). The overall sensitivity of canine detection was 97% (95% CI, 92 to 99) and even reached 100% (95% CI, 89 to 100) in asymptomatic individuals compared to NPS RT-PCR. The specificity was 91% (95% CI, 72 to 91), reaching 94% (95% CI, 90 to 97) for asymptomatic individuals. The sensitivity of canine detection was higher than that of nasopharyngeal antigen testing (97% CI: 91 to 99 versus 84% CI: 74 to 90, $p = 0.006$), but the specificity was lower (90% CI: 84 to 95 versus 97% CI: 93 to 99, $p = 0.016$).

Conclusions: Non-invasive detection of SARS-CoV-2 infection by canine olfaction could be one alternative to NPS RT-PCR when it is necessary to obtain a result very quickly according to the same indications as antigenic tests in the context of mass screening."

Euro Surveill: [Investigation of a COVID-19 outbreak on the Charles de Gaulle aircraft carrier, March to April 2020: a retrospective cohort study](#) (26 May 2022)

"Background: SARS-CoV-2 emergence was a threat for armed forces. A COVID-19 outbreak occurred on the French aircraft carrier Charles de Gaulle from mid-March to mid-April

2020. Aim To understand how the virus was introduced, circulated then stopped circulation, risk factors for infection and severity, and effectiveness of preventive measures.

Methods: We considered the entire crew as a cohort and collected personal, clinical, biological, and epidemiological data. We performed viral genome sequencing and searched for SARS-CoV-2 in the environment.

Results: The attack rate was 65% (1,148/1,767); 1,568 (89%) were included. The male:female ratio was 6.9, and median age was 29 years (IQR: 24-36). We examined four clinical profiles: asymptomatic (13.0%), non-specific symptomatic (8.1%), specific symptomatic (76.3%), and severe (i.e. requiring oxygen therapy, 2.6%). Active smoking was not associated with severe COVID-19; age and obesity were risk factors. The instantaneous reproduction rate (R_t) and viral sequencing suggested several introductions of the virus with 4 of 5 introduced strains from within France, with an acceleration of R_t when lifting preventive measures. Physical distancing prevented infection (adjusted OR: 0.55; 95% CI: 0.40-0.76). Transmission may have stopped when the proportion of infected personnel was large enough to prevent circulation (65%; 95% CI: 62-68).

Conclusion: Non-specific clinical pictures of COVID-19 delayed detection of the outbreak. The lack of an isolation ward made it difficult to manage transmission; the outbreak spread until a protective threshold was reached. Physical distancing was effective when applied. Early surveillance with adapted prevention measures should prevent such an outbreak."

PLoS Med: [Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: Update of a living systematic review and meta-analysis](#) (26 May 2022)

"Background: Debate about the level of asymptomatic Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection continues. The amount of evidence is increasing and study designs have changed over time. We updated a living systematic review to address 3 questions: (1) Among people who become infected with SARS-CoV-2, what proportion does not experience symptoms at all during their infection? (2) What is the infectiousness of asymptomatic and presymptomatic, compared with symptomatic, SARS-CoV-2 infection? (3) What proportion of SARS-CoV-2 transmission in a population is accounted for by people who are asymptomatic or presymptomatic?

Methods and findings: The protocol was first published on 1 April 2020 and last updated on 18 June 2021. We searched PubMed, Embase, bioRxiv, and medRxiv, aggregated in a database of SARS-CoV-2 literature, most recently on 6 July 2021. Studies of people with PCR-diagnosed SARS-CoV-2, which documented symptom status at the beginning and end of follow-up, or mathematical modelling studies were included. Studies restricted to people already diagnosed, of single individuals or families, or without sufficient follow-up were excluded. One reviewer extracted data and a second verified the extraction, with disagreement resolved by discussion or a third reviewer. Risk of bias in empirical studies

was assessed with a bespoke checklist and modelling studies with a published checklist. All data syntheses were done using random effects models. Review question (1): We included 130 studies. Heterogeneity was high so we did not estimate a mean proportion of asymptomatic infections overall (interquartile range (IQR) 14% to 50%, prediction interval 2% to 90%), or in 84 studies based on screening of defined populations (IQR 20% to 65%, prediction interval 4% to 94%). In 46 studies based on contact or outbreak investigations, the summary proportion asymptomatic was 19% (95% confidence interval (CI) 15% to 25%, prediction interval 2% to 70%). (2) The secondary attack rate in contacts of people with asymptomatic infection compared with symptomatic infection was 0.32 (95% CI 0.16 to 0.64, prediction interval 0.11 to 0.95, 8 studies). (3) In 13 modelling studies fit to data, the proportion of all SARS-CoV-2 transmission from presymptomatic individuals was higher than from asymptomatic individuals. Limitations of the evidence include high heterogeneity and high risks of selection and information bias in studies that were not designed to measure persistently asymptomatic infection, and limited information about variants of concern or in people who have been vaccinated.

Conclusions: Based on studies published up to July 2021, most SARS-CoV-2 infections were not persistently asymptomatic, and asymptomatic infections were less infectious than symptomatic infections. Summary estimates from meta-analysis may be misleading when variability between studies is extreme and prediction intervals should be presented. Future studies should determine the asymptomatic proportion of SARS-CoV-2 infections caused by variants of concern and in people with immunity following vaccination or previous infection. Without prospective longitudinal studies with methods that minimise selection and measurement biases, further updates with the study types included in this living systematic review are unlikely to be able to provide a reliable summary estimate of the proportion of asymptomatic infections caused by SARS-CoV-2."

Clin Infect Dis: [Early introduction and rise of the Omicron SARS-CoV-2 variant in highly vaccinated university populations](#) (25 May 2022)

"Background: The Omicron variant of SARS-CoV-2 is highly transmissible in vaccinated and unvaccinated populations. The dynamics governing its establishment and propensity towards fixation (reaching 100% frequency in the SARS-CoV-2 population) in communities remain unknown. In this work, we describe the dynamics of Omicron at three institutions of higher education (IHEs) in the greater Boston area.

Methods: We use diagnostic and variant-specifying molecular assays and epidemiological analytical approaches to describe the rapid dominance of Omicron following its introduction to three IHEs with asymptomatic surveillance programs.

Results: We show that the establishment of Omicron at IHEs precedes that of the state and region, and that the time to fixation is shorter at IHEs (9.5-12.5 days) than in the state (14.8

days) or region. We show that the trajectory of Omicron fixation among university employees resembles that of students, with a 2-3 day delay. Finally, we compare cycle threshold (Ct) values in Omicron vs. Delta variant cases on college campuses, and identify lower viral loads among college affiliates harboring Omicron infections.

Conclusions: We document the rapid takeover of the Omicron variant at IHEs, reaching near-fixation within the span of 9.5-12.5 days despite lower viral loads, on average, than the previously dominant Delta variant. These findings highlight the transmissibility of Omicron, its propensity to rapidly dominate small populations, and the ability of robust asymptomatic surveillance programs to offer early insights into the dynamics of pathogen arrival and spread."

Viruses: [Understanding the Driving Forces That Trigger Mutations in SARS-CoV-2: Mutational Energetics and the Role of Arginine Blockers in COVID-19 Therapy](#) (11 May 2022)

"SARS-CoV-2 is a global challenge due to its ability to mutate into variants that spread more rapidly than the wild-type virus. Because the molecular biology of this virus has been studied in such great detail, it represents an archetypal paradigm for research into new antiviral drug therapies. The rapid evolution of SARS-CoV-2 in the human population is driven, in part, by mutations in the receptor-binding domain (RBD) of the spike (S-) protein, some of which enable tighter binding to angiotensin-converting enzyme (ACE2). More stable RBD-ACE2 association is coupled with accelerated hydrolysis of furin and 3CLpro cleavage sites that augment infection. Non-RBD and non-interfacial mutations assist the S-protein in adopting thermodynamically favorable conformations for stronger binding. The driving forces of key mutations for Alpha, Beta, Gamma, Delta, Kappa, Lambda and Omicron variants, which stabilize the RBD-ACE2 complex, are investigated by free-energy computational approaches, as well as equilibrium and steered molecular dynamic simulations. Considered also are the structural hydropathy traits of the residues in the interface between SARS-CoV-2 RBD and ACE2 protein. Salt bridges and π - π interactions are critical forces that create stronger complexes between the RBD and ACE2. The trend of mutations is the replacement of non-polar hydrophobic interactions with polar hydrophilic interactions, which enhance binding of RBD with ACE2. However, this is not always the case, as conformational landscapes also contribute to a stronger binding. Arginine, the most polar and hydrophilic among the natural amino acids, is the most aggressive mutant amino acid for stronger binding. Arginine blockers, such as traditional sartans that bear anionic tetrazoles and carboxylates, may be ideal candidate drugs for retarding viral infection by weakening S-protein RBD binding to ACE2 and discouraging hydrolysis of cleavage sites. Based on our computational results it is suggested that a new generation of "supersartans", called "bisartans", bearing two anionic biphenyl-tetrazole pharmacophores, are superior to carboxylates in terms of their interactions with viral targets, suggesting their potential as drugs in the treatment of COVID-19. In Brief: This in silico study reviews our understanding

of molecular driving forces that trigger mutations in the SARS-CoV-2 virus. It also reports further studies on a new class of "supersartans" referred to herein as "bisartans", bearing two anionic biphenyltetrazole moieties that show potential in models for blocking critical amino acids of mutants, such as arginine, in the Delta variant. Bisartans may also act at other targets essential for viral infection and replication (i.e., ACE2, furin cleavage site and 3CLpro), rendering them potential new drugs for additional experimentation and translation to human clinical trials."

Treatments and Management

News in Brief

The NIH has updated its COVID-19 Treatment Guidelines, recommending against the use of colchicine for hospitalized patients, and making changes to the sections on critical care for adults, antithrombotic therapy, corticosteroids, and special considerations for people with cancer ([NIH](#)).

"U.S. doctors reconsider Pfizer's Paxlovid for lower-risk COVID patients" ([Reuters](#)).

"Pfizer's Paxlovid reduces COVID risk in seniors regardless of vaccine status -study" ([Reuters](#)).

"Coronavirus hasn't developed resistance to Paxlovid. How long can that last?" ([STAT](#))

Journal Articles

Ann Intern Med: [Effect of Molnupiravir on Biomarkers, Respiratory Interventions, and Medical Services in COVID-19: A Randomized, Placebo-Controlled Trial](#) (07 June 2022)

"Background: In the MOVE-OUT trial, molnupiravir showed a clinically meaningful reduction in the risk for hospitalization or death in adults with mild to moderate COVID-19 and risk factors for progression to severe disease.

Objective: To identify other potential clinical benefits of molnupiravir versus placebo.

Design: Secondary analysis of the randomized, double-blind, placebo-controlled phase 3 component of MOVE-OUT. (ClinicalTrials.gov: NCT04575597).

Setting: 107 sites globally.

Participants: 1433 nonhospitalized adults aged 18 years or older with mild to moderate COVID-19.

Intervention: Molnupiravir, 800 mg, or placebo every 12 hours for 5 days.

Measurements: Changes from baseline in C-reactive protein (CRP) concentration and oxygen saturation (Spo 2), need for respiratory interventions (including invasive mechanical ventilation), and need for medical services in all randomly assigned participants through day 29, and need for respiratory interventions and time to discharge in the subgroup of participants who were hospitalized after randomization.

Results: Participants receiving molnupiravir showed faster normalization of CRP and Spo 2, with improvements observed on day 3 of therapy, compared with placebo. Molnupiravir-treated participants had a decreased need for respiratory interventions versus placebo-treated participants (relative risk reduction [RRR], 34.3% [95% CI, 4.3% to 54.9%]), with similar findings in participants who were hospitalized after randomization (RRR, 21.3% [CI, 0.2% to 38.0%]). Hospitalized participants who received molnupiravir were discharged a median of 3 days before those who received placebo. Acute care visits (7.2% vs. 10.6%; RRR, 32.1% [CI, 4.4% to 51.7%]) and COVID-19-related acute care visits (6.6% vs. 10.0%; RRR, 33.8% [CI, 5.6% to 53.6%]) were less frequent in molnupiravir- versus placebo-treated participants.

Limitations: Some analyses were performed post hoc. Longer-term benefits of molnupiravir therapy were not evaluated. Participants were not immunized against SARS-CoV-2.

Conclusion: The findings suggest there are additional important clinical benefits of molnupiravir beyond reduction in hospitalization or death."

Clin Infect Dis: [Effectiveness of Paxlovid in Reducing Severe COVID-19 and Mortality in High Risk Patients](#) (02 June 2022)

"Background: Paxlovid was granted emergency use authorization for the treatment of mild to moderate COVID-19, based on the interim analysis of EPIC-HR trial. Paxlovid effectiveness needs to be assessed in a noncontrolled setting. In this study we used population-based real world data to evaluate the effectiveness of Paxlovid.

Methods: The database of the largest healthcare provider in Israel was used to identify all adults aged 18 years or older with first ever positive test for SARS-CoV-2 between January and February 2022, who were at high risk for severe COVID-19 and had no contraindications for Paxlovid use. Patients were included irrespective of their COVID-19 vaccination status. Cox hazard regression was used to estimate the 28 day HR for severe COVID-19 or mortality with Paxlovid examined as time-dependent variable.

Results: Overall, 180,351 eligible were included, of them only 4,737 (2.6%) were treated with Paxlovid, and 135,482 (75.1%) had adequate COVID-19 vaccination status. Both Paxlovid and adequate COVID-19 vaccination status were associated with significant decrease in the rate of severe COVID-19 or mortality with adjusted HR 0.54 (95% CI, 0.39-

0.75) and 0.20 (95% CI, 0.17-0.22), respectively. Paxlovid appears to be more effective in older patients, immunosuppressed patients, and patients with underlying neurological or cardiovascular disease (interaction p-value <0.05 for all). No significant interaction was detected between Paxlovid treatment and COVID-19 vaccination status.

Conclusions: This study suggests that in the era of omicron and in real life setting Paxlovid is highly effective in reducing the risk of severe COVID-19 or mortality."

JAMA Intern Med: [Racial and Ethnic Discrepancy in Pulse Oximetry and Delayed Identification of Treatment Eligibility Among Patients With COVID-19](#) (31 May 2022)

"Question: Are there systematic racial and ethnic biases in pulse oximetry among patients with COVID-19, and is there an association between such biases and unrecognized or delayed recognition of eligibility for oxygen threshold–specific therapy?

Findings: In this retrospective cohort study of 7126 patients with COVID-19, an analysis of 1216 patients with oxygen saturation levels that were concurrently measured by pulse oximetry and arterial blood gas demonstrated that pulse oximetry overestimated arterial oxygen saturation among Asian, Black, and Hispanic patients compared with White patients. Separately, among 6673 patients with pulse oximetry measurements and available covariate data, predicted overestimation of arterial oxygen saturation levels by pulse oximetry among 1903 patients was associated with a systematic failure to identify Black and Hispanic patients who were qualified to receive COVID-19 therapy and a statistically significant delay in recognizing the guideline-recommended threshold for initiation of therapy.

Meaning: The study results suggest that overestimation of arterial oxygen saturation levels by pulse oximetry occurs in patients of racial and ethnic minority groups with COVID-19 and contributes to unrecognized or delayed recognition of eligibility to receive COVID-19 therapies."

J Clin Med: [Age-Dependent Biomarkers for Prediction of In-Hospital Mortality in COVID-19 Patients](#) (10 May 2022)

"Background: Several biomarkers and models have been proposed to predict in-hospital mortality among COVID-19 patients. However, these studies have not examined the association in sub-populations. The present study aimed to identify the association between the two most common inflammatory biomarkers in the emergency department and in-hospital mortality in subgroups of patients.

Methods: A historical cohort study of adult patients who were admitted to acute-care hospital between March and December 2020 and had a diagnosis of COVID-19 infection. Data on age, sex, Charlson comorbidity index, white blood cell (WBC) count, C-reactive

protein (CRP), and in-hospital mortality were collected. Discrimination ability of each biomarker was observed and the CHAID method was used to identify the association in subgroups of patients.

Results: Overall, 762 patients (median age 70.9 years, 59.7% males) were included in the study. Of them, 25.1% died during hospitalization. In-hospital mortality was associated with higher CRP (median 138 mg/L vs. 85 mg/L, $p < 0.001$), higher WBC count (median 8.5 vs. 6.6 K/ μ L, $p < 0.001$), and higher neutrophil-to-lymphocyte ratio (NLR) (median 9.2 vs. 5.4, $p < 0.001$). The area under the ROC curve was similar among all biomarkers (WBC 0.643, NLR 0.677, CRP 0.646, $p > 0.1$ for all comparisons). The CHAID method revealed that WBC count was associated with in-hospital mortality in patients aged 43.1-66.0 years (< 11 K/ μ L: 10.1% vs. ≥ 11 K/ μ L: 27.9%), NLR in patients aged 66.1-80 years (≤ 8 : 15.7%, > 8 : 43.3%), and CRP in patients aged 80.1+ years (≤ 47 mg/L: 18.8%, 47.1-149 mg/L: 43.1%, and ≥ 149.1 : 71.7% mortality).

Conclusions: WBC, NLR, and CRP present similar discrimination abilities. However, each biomarker should be considered as a predictor for in-hospital mortality in different age groups."

Breakthrough Infections, Reinfections, and Coinfections

News in Brief

"You are going to get COVID again ... and again ... and again" ([Atlantic](#)).

"Welcome to the Great Reinfection — A repeat encounter with Covid used to be a rarity. But now that Omicron has changed the game, expect reinfections to be the new normal" ([Wired](#)).

Journal Articles

Virol J: [Herpesvirus and neurological manifestations in patients with severe coronavirus disease](#) (08 June 2022)

"Background: Certain clinical manifestations of coronavirus disease (COVID-19) mimic those associated with human herpesvirus (HHV) infection. In this study, we estimated the prevalence of herpesvirus in patients with COVID-19 and determined if coinfection is associated with poorer outcomes and neurological symptoms.

Methods: We analyzed samples of 53 patients diagnosed with COVID-19. The samples were evaluated for the presence of alphaherpesviruses, betaherpesviruses, and

gammaherpesviruses, and the viral loads were quantified using quantitative polymerase chain reaction (qPCR) method.

Results: Among the patients, in 79.2% had detection at least one type of herpesvirus. HHV-6 (47.2%), cytomegalovirus (43.3%), and HHV-7 (39.6%) showed the highest detection rates. Patients with a high severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) load were more likely to show herpes simplex virus 1 detection ($p = 0.037$). Among patients coinfecting with SARS-CoV-2 and HHVs, 26.4% showed central nervous system-associated neurological symptoms and herpetic manifestations. A statistically significant association was observed between neurological changes and HHV-6 detection ($p = 0.034$).

Conclusions: The findings showed a high prevalence of herpesvirus in patients with COVID-19. Furthermore, even though SARS-CoV-2 and HHV coinfection was not associated with poorer outcomes, the findings demonstrated the association between neurological symptoms and HHV-6 detection."

JAMA Netw Open: [Analysis of Postvaccination Breakthrough COVID-19 Infections Among Adults With HIV in the United States](#) (07 June 2022)

"Question: Are the rate and risk of COVID-19 breakthrough infections higher among vaccinated people with vs without HIV in the United States through December 31, 2021?

Findings: In this cohort study of 113 994 patients, risk of breakthrough infection was low overall (3.8%) but 28% higher in people with vs without HIV. The breakthrough rate was also higher in people with vs without HIV (55 cases per 1000 person-years vs 43 cases per 1000 person-years).

Meaning: The higher rate and risk of infection in people with HIV observed in this study suggests comprehensive inclusion of this population in recommendations for additional primary doses in immunocompromised groups."

AJR Am J Roentgenol: [Pneumonia Frequency and Severity in Patients With Symptomatic COVID-19: Impact of mRNA and Adenovirus Vector Vaccines](#) (01 June 2022)

"Background: Additional evidence of the role of COVID-19 vaccination in reducing pneumonia frequency and severity in the setting of breakthrough infection could help combat ongoing vaccine hesitancy.

Objective: To compare the frequency and severity of pneumonia on chest CT in patients with confirmed COVID-19 between unvaccinated patients and patients fully vaccinated by mRNA or adenovirus vector vaccines.

Methods: This retrospective single-center study included 467 patients (250 men, 217 women; mean age, 65 ± 17 years) who underwent chest CT between December 15, 2021, and February 18, 2022 during hospitalization for symptomatic COVID-19, confirmed by

reverse transcriptase-polymerase chain reaction assay. A total of 216 patients were unvaccinated, and 167 and 84 patients were fully vaccinated (defined as receipt of the second dose at least 14 days before COVID-19 diagnosis) by the BNT162b2 mRNA vaccine or the ChAdOx1-S adenovirus vector vaccine, respectively. Semi-quantitative CT severity scores (CT-SS; 0-25 scale) were determined; CT-SS of 0 indicated absence of pneumonia. Presence of bilateral involvement was assessed in patients with pneumonia. Associations were explored between vaccination status and CT findings.

Results: The frequency of an absence of pneumonia was 15% (32/216) in unvaccinated patients, 29% (24/84) in patients fully vaccinated with ChAdOx1-S vaccine, and 51% (85/167) in patients fully vaccinated with BNT162b2 vaccine (unvaccinated and ChAdOx1-S vs BNT162b2: $p < .001$; unvaccinated vs ChAdOx1: $p = .08$). Mean CT-SS was significantly higher in unvaccinated patients (9.7 ± 6.1) than in patients fully vaccinated with BNT162b2 (5.2 ± 6.1) or ChAdOx1-S (6.2 ± 5.9) vaccines (both $p < .001$). Full vaccination was significantly associated with CT-SS independent of patient age and sex (estimate = -4.46 ; $p < .001$). Frequency of bilateral lung involvement was significantly higher in unvaccinated patients (158/184, 86%) and in patients fully vaccinated with ChAdOx1-S vaccine (54/60, 90%) than in patients fully vaccinated with BNT162b2 vaccine (47/82, 57%) (both $p < .001$).

Conclusion: Pneumonia frequency and severity were lower in patients with full vaccination by mRNA and adenovirus vector vaccines experiencing breakthrough infections in comparison with unvaccinated patients. Clinical Impact: The visual observation by radiologic imaging of the protective effect of vaccination on lung injury in patients with breakthrough infections provides additional evidence supporting the clinical benefit of vaccination."

Long COVID and Other Post-Infectious Findings

News in Brief

"Expert panel shares best practices for managing patients with long COVID — 'We're learning as we go,' experts say" ([Medpage](#)).

"Are these Cocoa Krispies-loving hamsters a key to cracking long Covid?" ([STAT](#))

"Got long covid? Medical expertise is vital, and seniors should prepare to go slow" ([KHN](#)).

Opinion: "Long COVID in older adults: an elusive geriatric syndrome — We need to redefine the condition for better diagnosis and management" ([Medpage](#)).

Long Reads

"How long covid could change the way we think about disability" ([WP](#); includes audio option).

Special Reports and Other Resources

Preprints (not yet peer reviewed) from medRxiv:

- [A global systematic analysis of the occurrence, severity, and recovery pattern of long COVID in 2020 and 2021](#) (27 May 2022)
- [Generalizable Long COVID Subtypes: Findings from the NIH N3C and RECOVER Programs](#) (25 May 2022)

Journal Articles

Expert Rev Clin Immunol: [Is post-COVID syndrome an autoimmune disease?](#) (05 June 2022)

"Introduction: Coronavirus disease 2019 (COVID-19) causes a long-term and persistent condition with clinical features similar to previous virulent outbreaks and other epidemics. Currently, post-COVID syndrome (PCS) is recognized as a new entity in the context of SARS-CoV-2 infection. Though its pathogenesis is not completely understood, persistent inflammation from acute illness and the development of autoimmunity play a critical role in its development. As the pandemic develops, the increasing latent and overt autoimmunity cases indicate that PCS is at the intersection of autoimmunity.

Areas covered: The mechanisms involved in the emergence of PCS, their similarities with post-viral and post-care syndromes, its inclusion in the spectrum of autoimmunity and possible targets for its treatment.

Expert opinion: An autoimmune phenomenon plays a major role in most causative theories explaining PCS. Due to the wide scope of symptoms and pathophysiology associated with PCS, there is a need for both PCS definition and classification criteria (including severity scores). Longitudinal and controlled studies are necessary to better understand this new entity, and to confirm that PCS is the chronic phase of COVID-19 as well as to find what additional factors participate into its development. With the high prevalence of COVID-19 cases worldwide, together with the current evidence on latent autoimmunity in PCS, we may observe an increase of autoimmune diseases (ADs) in the coming years. Vaccination's effect on the development of PCS and ADs will also receive attention in the future. Health and social care services need to develop a new framework to deal with PCS."

PM&R: [Multi-Disciplinary Collaborative Consensus Guidance Statement on the Assessment and Treatment of Cardiovascular Complications in Patients with Post-Acute Sequelae of SARS-CoV-2 Infection \(PASC\)](#) (03 June 2022)

"More than 100 symptoms have been reported with PASC. (1) The more common symptoms include fatigue, shortness of breath, chest discomfort / pains, palpitations, cognitive dysfunction ("brain fog"), sleep disorders, fevers, gastrointestinal symptoms,

anxiety, and depression. (1) It is important to recognize that individuals who did not have acute COVID-19 symptoms in the days or weeks after they were infected can develop PASC symptoms and conditions weeks to months after acute infection. These post-COVID conditions have also been reported using the terms long COVID, long-haul COVID, post-acute COVID-19, long-term effects of COVID, or chronic COVID. (2) This guidance statement uses the terminology PASC and focuses on the assessment and treatment of cardiovascular complications of PASC."

JBJS Rev: [What Do We Need to Know About Musculoskeletal Manifestations of COVID-19?: A Systematic Review](#) (03 June 2022)

"»: COVID-19 is a disease that is challenging science, health-care systems, and humanity. An astonishingly wide spectrum of manifestations of multi-organ damage, including musculoskeletal, can be associated with SARS-CoV-2.

»: In the acute phase of COVID-19, fatigue, myalgia, and arthralgia are the most common musculoskeletal symptoms.

»: Post-COVID-19 syndrome is a group of signs and symptoms that are present for >12 weeks. The associated musculoskeletal manifestations are fatigue, arthralgia, myalgia, new-onset back pain, muscle weakness, and poor physical performance.

»: Data on COVID-19 complications are growing due to large absolute numbers of cases and survivors in these 2 years of the pandemic. Additional musculoskeletal manifestations encountered are falls by the elderly, increased mortality after hip fracture, reduced bone mineral density and osteoporosis, acute sarcopenia, rhabdomyolysis, Guillain-Barré syndrome, muscle denervation atrophy, fibromyalgia, rheumatological disease triggering, septic arthritis, adhesive capsulitis, myositis, critical illness myopathy, onset of latent muscular dystrophy, osteonecrosis, soft-tissue abscess, urticarial vasculitis with musculoskeletal manifestations, and necrotizing autoimmune myositis.

»: A wide range of signs and symptoms involving the musculoskeletal system that affect quality of life and can result in a decrease in disability-adjusted life years. This powerful and unpredictable disease highlights the importance of multimodality imaging, continuing education, and multidisciplinary team care to support preventive measures, diagnosis, and treatment."

Pregnancy, Postpartum Period, and Women's Health

Journal Articles

JAMA Netw Open: [Frequency and Outcomes of Ipsilateral Axillary Lymphadenopathy After COVID-19 Vaccination](#) (07 June 2022)

"This case series reports on the frequency and outcomes of breast imaging--identified ipsilateral axillary lymphadenopathy after recent COVID-19 vaccination among women....

With more than 70% of US adults receiving the COVID-19 vaccine, evidence-based guidelines for postvaccination IAL are necessary. Although the reported frequency of IAL varies (3%-44%), our data on the frequency of IAL (10%) are similar to those reported for patients in clinical trials (14%)."

Clin Infect Dis: [Maternal and perinatal outcomes associated with SARS-CoV-2 infection during pregnancy, Florida, 2020-2021: A retrospective cohort study](#) (08 June 2022)

"Background: The objective was to estimate risk of SARS-CoV-2 infection in pregnancy and assess adverse maternal and perinatal outcomes.

Methods: We used a population-based, retrospective cohort of all pregnancies with a live birth or fetal death in Florida from March 1, 2020 to April 30, 2021. COVID-19 case reports were matched to vital registries. Outcomes assessed were risk of infection in pregnancy, preterm birth, maternal or neonatal admission to an intensive care unit (ICU), perinatal or fetal death, and maternal death. Modified Poisson and multinomial logistic regression models were used to derive relative risk estimates.

Results: Of 234,492 women with a live birth or fetal death during the study period, 12,976 (5.5%) were identified with COVID-19 during pregnancy. Risk factors for COVID-19 in pregnancy included Hispanic ethnicity (relative risk [RR] = 1.89), Black race (RR = 1.34), being unmarried (RR = 1.04), and being overweight or obese pre-pregnancy (RR = 1.08-1.32). COVID-19 during pregnancy was associated with preterm birth (RR = 1.31), Cesarean delivery (RR = 1.04), and neonatal (RR = 1.17) and maternal (RR = 3.10) ICU admission; no association was found with increased risk of perinatal (RR = 0.72) or fetal death (RR = 0.86). Women infected during any trimester showed increased risk of preterm birth. Fourteen maternal deaths were identified among COVID-19 cases; of those who died 12 were obese. The death rate per 10,000 was 22.09 among obese and 1.22 among non-obese gravida with COVID-19 during pregnancy (RR = 18.99, P = 0.001).

Conclusions: Obesity is a risk factor for SARS-CoV-2 infection in pregnancy and for more severe COVID-19 illness among pregnant women. SARS-CoV-2 infection is associated with preterm birth."

JAMA Intern Med: [Association of COVID-19 Vaccination During Pregnancy With Incidence of SARS-CoV-2 Infection in Infants](#) (01 June 2022)

"Question: Is maternal COVID-19 vaccination during the second or third trimester of pregnancy associated with reduced risk of COVID-19 within the first 4 months of life in their infants?

Findings: In this register-based cohort study of all live-born infants in Norway, there was a lower incidence of a positive SARS-CoV-2 test result in infants born to women vaccinated with a messenger RNA vaccine during pregnancy. The risk was lower during the period dominated by the Delta variant than during the Omicron-dominated period.

Meaning: The study results suggest that maternal COVID-19 vaccination during pregnancy could protect against infant SARS-CoV-2 infection in the early months of life."

Pediatric Population

News in Brief

The NIH has updated its COVID-19 Treatment Guidelines to include a section on critical care for children ([NIH](#)).

"White House says kids under 5 could get COVID-19 vaccines by June 21" ([Hill](#)).

Podcast: "Covid-19 is leaving millions of orphaned children behind" ([STAT](#)).

Pandemic disrupted learning for U.S. teens, but not evenly, poll shows" ([WP](#); see also: [Pew survey report](#)).

Beyond COVID

"GSK announces US FDA approval of Priorix for the prevention of measles, mumps and rubella in individuals 12 months of age and older" ([GSK](#)).

Journal Articles

JAMA Netw Open: [Neurodevelopmental Outcomes at 1 Year in Infants of Mothers Who Tested Positive for SARS-CoV-2 During Pregnancy](#) (09 June 2022)

"Question: Is COVID-19 exposure in utero associated with increased risk for neurodevelopmental disorders in the first year of life?

Findings: In this cohort study of 7772 infants delivered during the COVID-19 pandemic, those born to the 222 mothers with a positive SARS-CoV-2 polymerase chain reaction test during pregnancy were more likely to receive a neurodevelopmental diagnosis in the first 12 months after delivery, even after accounting for preterm delivery.

Meaning: These preliminary findings suggest that COVID-19 exposure may be associated with neurodevelopmental changes and highlight the need for prospective investigation of outcomes in children exposed to COVID-19 in utero."

JAMA Pediatr: [Risk and Phenotype of Multisystem Inflammatory Syndrome in Vaccinated and Unvaccinated Danish Children Before and During the Omicron Wave](#) (08 June 2022)

"This cohort study investigates the risk of multisystem inflammatory syndrome after SARS-CoV-2 infection in vaccinated and unvaccinated children before and during the Omicron wave in Denmark....

We found the risk of MIS-C after SARS-CoV-2 infection during the Omicron wave substantially lower compared with previous SARS-CoV-2 variants. This could be explained by a reduced ability of Omicron to trigger hyperinflammation as it is phylogenetically different and associated with an increased immune escape. The lower risk could also partly be explained by a reduced risk after reinfection, although only 6% of our included infected individuals had confirmed reinfection, and such a reduced risk after reinfection has not yet been reported."

JAMA Pediatr: [Use of Race in Pediatric Clinical Practice Guidelines: A Systematic Review](#) (06 June 2022)

"Question: How is race used in pediatric clinical practice guidelines?

Findings: In this systematic review including 126 pediatric clinical practice guidelines, race was frequently used in pediatric clinical practice guidelines in a way that could negatively affect health care inequities.

Meaning: The use of race in pediatric national guidelines should be improved to prevent the perpetuation of racial inequity and health care inequities."

Long COVID

Ital J Pediatr: [Long COVID-19 in children: an Italian cohort study](#) (03 June 2022)

"Background: Long COVID-19 syndrome is a complex of symptoms that occurs after the acute SARS-CoV-2 infection, in the absence of other possible diagnoses. Studies on Long COVID-19 in pediatric population are scanty and heterogeneous in design, inclusion criteria, outcomes, and follow-up time. The objective of the present study is to assess the

prevalence of Long COVID-19 syndrome in a cohort of Italian pediatric primary care patients, observed for a period of time of 8 to 36 weeks from healing. Prevalence was also assessed in a cohort of pediatric patients hospitalized during acute infection.

Methods: Data concerning 629 primary care patients with previous acute SARS-CoV-2 infection were collected by a questionnaire filled in by Primary Care Pediatrician (PCP). The questionnaire was administered to patients by 18 PCPs based in 8 different Italian regions from June to August 2021. Data concerning 60 hospitalized patients were also collected by consultation of clinical documents.

Results: Cumulative incidence of Long COVID-19 resulted to be 24.3% in primary care patients and 58% in hospitalized patients. The most frequently reported symptoms were abnormal fatigue (7%), neurological (6.8%), and respiratory disorders (6%) for the primary care cohort. Hospitalized patients displayed more frequently psychological symptoms (36.7%), cardiac involvement (23.3%), and respiratory disorders (18.3%). No difference was observed in cumulative incidence in males and females in both cohorts. Previous diseases did not influence the probability to develop Long COVID-19. The prevalence of Long COVID-19 was 46.5% in children who were symptomatic during acute infection and 11.5% in asymptomatic ones. Children aged 0 to 5 years had a greater risk to develop respiratory symptoms, while adolescents (aged 11-16 years) had a greater risk to develop neurological and psychological Long COVID-19 symptoms.

Conclusions: Our study demonstrates that Long COVID-19 is a reality in pediatric age and could involve even patients with mild or no acute symptoms. The results stress the importance of monitoring primary care pediatric patients after acute COVID-19 infection and the relevance of vaccination programs in pediatric population, also in order to avoid the consequences of Long COVID-19 syndrome."

Front Pediatr: [Post COVID-19 Condition in Children and Adolescents: An Emerging Problem](#) (11 May 2022)

"The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection became a pandemic in 2020 and by March 2022 had caused more than 479 million infections and 6 million deaths worldwide. Several acute and long-term symptoms have been reported in infected adults, but it remains unclear whether children/adolescents also experience persistent sequelae. Hence, we conducted a review of symptoms and pathophysiology associated with post-coronavirus disease 2019 (post-COVID-19) condition in children and adolescents. We reviewed the scientific literature for reports on persistent COVID-19 symptoms after SARS-CoV-2 infection in both children/adolescents and adults from 1 January 2020 to 31 March 2022 (based on their originality and relevance to the broad scope of this review, 26 reports were included, 8 focused on adults and 18 on children/adolescents). Persistent sequelae of COVID-19 are less common in

children/adolescents than in adults, possibly owing to a lower frequency of SARS-CoV-2 infection and to the lower impact of the infection itself in this age group. However, cumulative evidence has shown prolonged COVID-19 to be a clinical entity, with few pathophysiological associations at present. The most common post-COVID-19 symptoms in children/adolescents are fatigue, lack of concentration, and muscle pain. In addition, we found evidence of pathophysiology associated with fatigue and/or headache, persistent loss of smell and cough, and neurological and/or cardiovascular symptoms. This review highlights the importance of unraveling why SARS-CoV-2 infection may cause post-COVID-19 condition and how persistent symptoms might affect the physical, social, and psychological well-being of young people in the future."

Healthcare Workers

News in Brief

Beyond COVID

"Police: Tulsa gunman targeted surgeon he blamed for pain" ([AP](#)).

"Police ID suspect in attack on doctor, nurses at LA hospital" ([AP](#)).

"AMA, FDA launch continuing med ed course on dietary supplements" ([AMA](#); see also: [FDA website for content](#)).

Long read: "What the end of Roe v. Wade will mean for the next generation of obstetricians" ([New Yorker](#)).

Journal Articles

JAMA Netw Open: [Perceptions and Use of Telehealth Among Mental Health, Primary, and Specialty Care Clinicians During the COVID-19 Pandemic](#) (07 June 2022)

"Question: Are clinician perceptions of telehealth quality associated with use?

Findings: In this survey study of 866 mental health (MH), primary care (PC), and specialty care (SC) clinicians, MH clinicians rated the quality of video care the highest and were more likely to prefer video over phone when providing care for patients remotely; PC and SC clinicians were more likely to endorse challenges of video care. Findings aligned with utilization rates, with MH clinicians conducting significantly more video visits than PC and SC clinicians.

Meaning: These findings suggest that specialty-specific differences in clinician perceptions of telehealth were associated with actual use."

NEJM: [Racial and Ethnic Diversity of U.S. Residency Programs, 2011-2019](#) (02 June 2022)

Letter: "Our data show that racial and ethnic representation in surgical and nonsurgical residency programs has not substantially improved in the past decade and continues to lag behind the changing demographic characteristics of the U.S. population. Before meaningful change can be made at the residency level, further work must be done to characterize the problem. Underrepresentation must be addressed at the medical school level, given that the demographic characteristics of students in residency programs mirror such trends. In addition, we must determine how effectively medical schools are recruiting URiM applicants. Answering such questions will allow for more effective targeting of initiatives and resources."

JAMA Pediatr: [Association of Mistreatment and Discrimination With Medical School Attrition](#) (31 May 2022)

"Medical students who reported mistreatment and discrimination in the first 2 years of medical school were significantly more likely to subsequently leave medical school."

Eur J Emerg Med: [Burnout in emergency medicine professionals after 2 years of the COVID-19 pandemic: a threat to the healthcare system?](#) (27 May 2022)

"Background: Burnout is a common problem among healthcare professionals (HCPs), in particular young doctors and nurses working in emergency medical services. The coronavirus disease 2019 (COVID-19) pandemic has generated a substantial increase in the workload of those working in front-line services, and there is evidence of physical and mental distress among professionals that may have caused an increase in burnout.

Objective: The objective of the study was to evaluate the level of burnout in the different professionals of emergency medical services.

Design and participants: In January and February 2022, we conducted an online survey based on the Abbreviate Maslach inventory with the addition of three questions focused on possible modifying factors. The survey was disseminated to HCP via the list of European Society for Emergency Medicine contacts.

Outcome measures: The analysis was based on two of the three elements of the Maslach burnout concept, 'depersonalisation', 'emotional exhaustion', and 'personal accomplishment'. Overall burnout was defined when at least one of the two elements 'depersonalisation' or 'emotional exhaustion' reached the level of high burnout.

Results: The number of responders was 1925, 84% of which were physicians, 12% nurses, and 2% paramedics. Burnout was present in 62% of all responders. A high burnout level was

reported for depersonalisation, emotional exhaustion, and personal accomplishment in 47%, 46%, and 48% of responders, respectively. Females reported a higher proportion of burnout compared with males 64% vs. 59%, difference -6% [95% confidence interval CI, -8 to -1.9], and nurses higher than physicians, 73% vs. 60%, difference -13 (95% CI, -18.8 to -6). Less experienced professionals reported higher levels of burnout: those with less than 5 years of experience the burnout level was 74% compared with the group with more than 10 years, 60%, difference -26% (95% CI, -32 to -19.5). Reported frequent understaffing situations were associated with a higher risk of burnout: 70% vs. 37%, difference -33% (95% CI, -41 to -25). Burnout was associated with a higher risk of desire to change the workplace: 87% vs. 40%, difference -47% (95% CI, -52 to -42). Survey responders reported having access to support programmes in 41% of cases.

Conclusion: In this study, there is a high reported level of burnout among emergency HCPs. Several risk factors were identified such as being understaffed, female, or having less experience. HCPs with burnout thought more frequently about leaving the workplace, posing a threat to healthcare systems."

Mental Health and Wellness

Journal Articles

JAMA Netw Open: [Clinical and Financial Outcomes Associated With a Workplace Mental Health Program Before and During the COVID-19 Pandemic](#) (08 June 2022)

"Question: Is participation in a comprehensive employer-sponsored mental health benefit associated with reduced symptoms for employees and positive financial return on investment for employers?"

Findings: In this cohort study of 1132 employees participating in a workplace mental health program from 66 employers in the US, participants reported reduced symptoms of depression and anxiety. The program provided a positive return on investment for all salaries above the federal minimum wage.

Meaning: Results of this study suggest that employer-sponsored, evidence-based workplace mental health programs can be beneficial for both employers and employees."

J Psychiatr Res: [Loneliness in U.S. military veterans during the COVID-19 pandemic: A nationally representative, prospective cohort study](#) (23 May 2022)

"Loneliness was deemed a behavioral epidemic even prior to the COVID-19 pandemic. The COVID-19 pandemic and the subsequent social distancing policy measures have raised

concerns about increased social isolation and loneliness, especially in vulnerable populations such as military veterans. However, little is known about the impact of the pandemic on longitudinal changes in loneliness in veterans, and potential protective psychosocial factors that may mitigate loneliness in this population. We analyzed data from the 2019-2020 National Health and Resilience in Veterans Study, which surveyed a nationally representative, prospective cohort of 3,078 US veterans before and 1-year into the pandemic. Prevalence, and risk and protective factors associated with changes in loneliness were examined. Results revealed that the prevalence of loneliness decreased over the study period-17.3% pre-pandemic to 15.9% peri-pandemic ($p = 0.032$). A total of 5.4% ($n = 164$) of veterans reported increased loneliness, 6.4% ($n = 196$) decreased loneliness, and 10.6% ($n = 325$) persistent loneliness during the pandemic. Multivariable logistic regression models indicated that not being married/partnered, and scoring lower on pre-pandemic measures of purpose in life and cognitive functioning were most strongly associated with increased loneliness. Pre-pandemic psychiatric disorder, unpartnered marital status, and pandemic-related social restriction and financial stressors were most strongly associated with persistent loneliness. Collectively, these results suggest that, contrary to concerns, the prevalence of loneliness subtly decreased one year into the pandemic. Veterans who are not partnered, have pre-existing psychiatric conditions, and endorse more COVID-related stressors may be at higher risk for experiencing loneliness during the pandemic. Interventions that promote social connectedness, as well as that target the aforementioned risk and protective factors, may help mitigate loneliness in veterans."

Other Infectious Diseases and Public Health Threats

News in Brief

"Here's where dangerous ticks are spreading across the US — and what to do about them" ([Vox](#)).

"There's still no HIV vaccine. The science behind coronavirus shots may help ([WP](#)).

WOAH: The WHO has rebranded its Office International des Epizooties (OIE) to the [World Organisation for Animal Health](#).

Food Issues

The FDA is tracking an outbreak of hepatitis A linked to organic strawberries ([FDA](#)) and issued a voluntary recall of cheeses contaminated with *Listeria monocytogenes* ([FDA](#)).

The CDC is looking into *Salmonella* outbreak due to peanut butter ([CDC](#)).

Special Topic: Monkeypox

News in Brief

As of Thursday 09 June 2022, there are over 1350 cases across 31 countries, with 44 confirmed in the US ([CDC](#)).

"Major US cities report new monkeypox cases" ([CIDRAP](#)).

Genetics and Epidemiology

Evidence from genetic testing of recent monkeypox cases suggest that it has been spreading silently for at least the past 5 years ([CNN](#)).

"Genetic data indicate at least two separate monkeypox outbreaks underway, suggesting wider spread" ([STAT](#)).

"Experts: Monkeypox highlights animal-human interface threats" ([CIDRAP](#)).

"Concern grows that human monkeypox outbreak will establish virus in animals outside Africa — New 'reservoirs' could make outbreaks common and spawn new variant" ([Science](#)).

Understanding the Outbreak

"Monkeypox outbreaks: 4 key questions researchers have. Researchers are racing to understand the latest monkeypox outbreaks — from their origins to whether they can be contained" ([Nature](#)).

"How bad could the monkeypox outbreak get? Health experts are optimistic monkeypox can be contained. Here's why, and where it could go wrong" ([Vox](#)).

"WHO: Monkeypox won't turn into pandemic, but many unknowns" ([AP](#)).

"'Nobody wants to mess this up': A WHO official weighs in on the challenges of responding to monkeypox" ([STAT](#)).

Exposure and Treatment

"Monkeypox patients should abstain from sex while symptomatic, U.K. says" ([WP](#)).

"Abbott developing test for monkeypox" ([Reuters](#)).

"US is offering vaccines to certain people exposed to monkeypox. Here's what you should know" ([CNN](#)).

"Monkeypox vaccination begins — can the global outbreaks be contained?" ([Nature](#))

"How much medicine does the U.S. actually have to fight monkeypox?" ([STAT](#))

Lessons Learned

"Monkeypox can look different than what doctors thought. Here's what they're learning" ([NPR](#)).

"How the hard lessons of the AIDS crisis are shaping the response to the monkeypox outbreak" ([STAT](#)).

Journal Articles

MMWR: [Monkeypox Outbreak — Nine States, May 2022](#) (early release 03 June 2022)

"What is already known about this topic? Monkeypox, a rare disease caused by infection with *Monkeypox virus*, is endemic in several Central and West African countries. Cases in persons outside Africa are often linked to international travel or imported animals.

What is added by this report? CDC is tracking multiple reported U.S. monkeypox cases, and monitoring cases in persons in countries without endemic monkeypox and with no known travel links to an endemic area; current epidemiology suggests person-to-person community spread.

What are the implications for public health practice? CDC urges health departments, clinicians, and the public to remain vigilant, institute appropriate infection prevention and control measures, and notify public health authorities of suspected cases to reduce disease spread."

MMWR: [Use of JYNNEOS \(Smallpox and Monkeypox Vaccine, Live, Nonreplicating\) for Preexposure Vaccination of Persons at Risk for Occupational Exposure to Orthopoxviruses: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022](#) (03 June 2022)

"What is already known about this topic? In 2015, the Advisory Committee on Immunization Practices (ACIP) recommended preexposure prophylaxis with ACAM2000, a replication-competent live virus *Vaccinia virus* vaccine, for certain U.S. persons at risk for occupational exposure to orthopoxviruses.

What is added by this report? In 2019, JYNNEOS, a replication-deficient live *Vaccinia virus* vaccine was licensed in the United States. On November 3, 2021, ACIP voted to recommend JYNNEOS preexposure prophylaxis as an alternative to ACAM2000 for certain persons at risk for exposure to orthopoxviruses.

What are the implications for public health practice? A second vaccine is now available for persons for whom vaccination against orthopoxvirus infections is recommended. Potential vaccinees should weigh the risks and benefits of each vaccine when deciding which to receive."

Euro Surveill: (rapid communications, 02 June 2022)

- [Community transmission of monkeypox in the United Kingdom, April to May 2022](#)
- [Monkeypox infection presenting as genital rash, Australia, May 2022](#)
- [Ongoing monkeypox virus outbreak, Portugal, 29 April to 23 May 2022](#)
- [Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022](#)

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